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Interactive Effects of Anti-Cardiovascular Disease Drugs and Anti-Osteoporosis Drugs on Two Diseases

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Abstract: Cardiovascular disease (CVD) and osteoporosis are common diseases in the middle-aged and elderly population, and the number of people affected by these two diseases has been steadily increasing against the background of a deepening global ageing population. The relationship between cardiovascular diseases and osteoporosis is complex, especially whether the related therapeutic drugs affect the development of the other disease while acting on one disease has become a hot research topic in the medical field. The purpose of this paper is to summarise the intrinsic connection between cardiovascular diseases and osteoporosis by systematically combing the authoritative literature at home and abroad in recent years, and to comprehensively analyse the mechanism of action of anti-cardiovascular disease and osteoporosis drugs, and to explore the influence of the therapeutic drugs for one disease on the other disease. This will provide strong support for clinicians to formulate more scientific and reasonable comprehensive treatment plans, and thus promote the progress and development of cardiovascular disease, osteoporosis and their co-morbidities management.

Keywords: Osteoporosis; Cardiovascular Disease; Beta-blockers; Statins; Renin-angiotensin System Inhibitors; Calcium Antagonists; Nitrates; Thiazide Diuretics; Vitamin D.

1. Introduction

Osteoporosis (OP) is a systemic skeletal disease closely associated with ageing, characterised by low bone mass and degeneration of bone microarchitecture, leading to increased bone fragility and increased fracture risk. The World Health Organisation reports that more than 200 million people worldwide are affected by OP [1] , making OP a major health problem worldwide.

Cardiovascular disease (CVD) is a series of diseases involving the heart and blood vessels, including but not limited to vascular disease, peripheral arterial disease, stroke, hypertension and atherosclerosis, as well as a variety of heart diseases such as heart failure and coronary heart disease, and is a major contributor to premature death and disability of human beings, according to the World Heart Report 2023 , CVD causes up to 20.5 million deaths, accounting for approximately one-third of all global deaths, and the global incidence continues to rise [2] , a trend that not only places a significant burden on patients and their families, but also puts pressure on the entire healthcare system.

The prevalence of OP and CVD increases with age, and there is a potential common mechanistic link between these two diseases [3,4] , and it is more common to see patients clinically suffering from both diseases. Currently, drugs for CVD and anti-OP drugs are widely used in clinical practice. Drugs for CVD affect bone metabolic homeostasis while acting on the cardiovascular system, and anti-OP drugs affect cardiovascular health while regulating bone homeostasis [3] . However, there is still much debate about the effects of treating one disease on another. Therefore, it is necessary to understand the effects of anti-OP drugs on cardiovascular metabolism, and anti-CVD drugs on bone metabolism, which are described in the following review.

2. Impact of anti-CVD drugs on OPs

2.1. Beta-blockers

Beta-blockers are a type of drug that selectively binds to beta-adrenergic receptors, thereby antagonising the agonistic effects of neurotransmitters and catecholamines on beta receptors. They are mostly used clinically to lower blood pressure, slow heart rate, inhibit myocardial contraction, prevent sudden death, and reduce mortality in patients with heart failure [5-7] . When sympathetic hypoplasia occurs, it is accompanied by a decrease in bone resorption and a significant enhancement of bone formation [8,9] . Beta-blockers, which block the effects of endogenous catecholamines on beta-adrenergic receptors, are thought to have a potential therapeutic role in OP.

Hijazi and Alourfi found [10] that hypertensive women taking the beta blocker had significantly increased mean total lumbar spine bone mineral density compared to women not taking the beta blocker . Nevola et al. [11] demonstrated a correlation between beta blockers and increased bone mineral density and reduced risk of fracture with respect to molecular mechanisms. Takeda et al. [12] the study found that propranolol, a beta-blocker, significantly reduced bone effects triggered by factors such as leptin and tail suspension in the brain by antagonising the function of the sympathetic nervous system. However, a retrospective study conducted in Korea involving 527,500 patients with essential hypertension noted that beta-blockers may increase the risk of fractures [13] . There is still a need for in-depth scientific research and

conclusive evidence to verify the effects of beta-blockers on osteoporosis.

2.2. Statins

Statins, as specific inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, occupy an unassailable central position in the field of lipid-lowering therapy for CVD patients. Statins precisely intervene in the cholesterol synthesis pathway within the hepatocyte, significantly cutting the concentration of total and LDL cholesterol in the serum [14] . Based on this mechanism, statins play a crucial role in reducing the risk of death in patients with CVD, and remain the cornerstone of dyslipidaemia therapy even as new drugs emerge [15] . In addition, statins have demonstrated significant anti-inflammatory properties, a unique biological effect that may provide novel therapeutic ideas and directions for the treatment of diseases closely related to inflammation.

As early as 1999, Mundy et al. [16] revealed the mechanism by which statin lipid-lowering drugs enhance bone morphogenetic protein (BMP)-2 gene expression. This finding was validated not only in isolated bone models but also in intact murine bone tissue, clearly demonstrating a significant positive effect of statins on bone formation. This was further reinforced by two subsequent meta-analyses, which revealed a significant role for statins in enhancing bone mineral density while significantly reducing the risk of osteoporotic fracture [17,18] . In addition, the study by Leutner et al.([19]) provided an insight into the dose-dependence of statins in the treatment of OP, suggesting that when evaluating a patient's risk of OP, it is important to consider whether or not he or she is receiving statin therapy, and to carefully analyse the type of statin used and the specific dosage.

The complex mechanisms of action of statins on bone metabolism are now becoming clear. These mechanisms cover multiple levels, including but not limited to: promoting osteoblast proliferation and new bone formation, accelerating osteoblast differentiation and maturation [20] ; preventing bone loss; reducing osteoblast apoptosis; decreasing FPP and GGPP synthesis, which creates a favourable environment for osteoblast differentiation; and curbing osteoclastogenesis, which further safeguards the health of bones [21] .

However, it is important to be wary that not all statins work equally well in terms of bone health. For example, one study found that pravastatin and fluvastatin did not show significant efficacy in the prevention and treatment of osteoporosis [22] , suggesting that there may be differential mechanisms of action of different statins in the bone conversion process.

2.3. Renin-angiotensin System Inhibitors

Inhibitors of the renin-angiotensin system, a class of antihypertensive drugs widely used in clinical practice, encompass two major classes: angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor antagonists (Angiotensin II Receptor Blocker (ARB). The core mechanism of ACEIs is to inhibit circulating and tissue angiotensin-converting enzyme activity, thereby reducing angiotensin II production. At the same time, by inhibiting bradykininase activity and reducing the degradation of bradykinin, they improve cardiomyocyte remodelling, insulin resistance and significantly reduce urinary protein.ARB drugs, on the other hand, effectively curb the vasoconstrictive effect of angiotensin II by selectively acting on the angiotensin II receptor (AT1 type).

Local hyperactivation of the renin-angiotensin system in bone tissue may be one of the key mechanisms in the development of osteoporosis [23] . In this over-activated state, the differentiation and maturation of osteoblasts and osteoclasts can be regulated through a variety of pathways, which in turn affects their functions, leading to a decrease in bone formation and an increase in bone resorption, and ultimately triggering osteoporosis [24] . Clinical studies have shown that ACEI intervention can effectively increase bone density and reduce fracture risk. In the treatment for menopausal hypertensive women, patients using this drug were able to effectively inhibit physiological bone loss compared to patients not using the ACEI drug fosinopril [25] . Zhang [26] et al.'s study has also further demonstrated that overactivation of the renin-angiotensin system locally in the bone tissue does lead to reduced bone formation and decreased bone mass, thus revealing that one of the important mechanisms of OP occurrence. In addition, several studies have also shown that in the treatment of hypertension, the application of RAS inhibitors not only effectively reduced blood pressure, but also increased bone mass and alleviated OP symptoms in patients, which once again proved the great pharmacological value of RAS inhibitors in the treatment of osteoporosis [2,27] .

2.4. Calcium Antagonists

Calcium antagonists have been proven effective in the treatment of acute hypertension since the 1960s and have subsequently become an important pillar in the treatment of hypertensive disorders. These drugs effectively reduce intracellular calcium ion concentration by precisely blocking vascular smooth muscle calcium in-flow, thereby reducing intravascular resistance and achieving a significant vasodilatory effect, which in turn leads to a return of blood pressure to normal levels. They have also demonstrated excellent performance in cardiovascular protection.

The common calcium channel blockers nifedipine, amlodipine, and felodipine have demonstrated favourable therapeutic effects on OP.A retrospective cohort analysis by Chang et al.([28]) showed a significant reduction in the risk of OP in patients treated with nifedipine irrespective of differences in gender or age. The experimental results of Ushijima K et al.([29]) , on the other hand, showed that amlodipine effectively elevated bone mineral density in 2-month-old hypertensive male rats by directly inhibiting osteoclast function and parathyroid hormone secretion, effectively elevated the BMD of femur in 2-month-old hypertensive male rats. The study of Menger et al.([30]) further found that the levels of bone morphogenetic protein-2 and vascular endothelial growth factor were significantly increased in 12-week-old to 16-week-old mice after 5-week oral administration of amlodipine.

Despite the fact that calcium antagonists may negatively affect bone metabolism by blocking the calcium ion-mediated bone synthesis and metabolism pathways, thus impacting bone mineralization and strength, their role in bone remodeling functions has gradually been confirmed. With further research, the application prospects of calcium antagonists in the fields of cardiovascular and bone health are expected to become even broader.

2.5. Nitrate Drugs

Nitrates provide strong support for the treatment of a wide

range of CVDs with their remarkable vascular smooth muscle relaxation effects, especially in the vascular system. These drugs can not only effectively dilate blood vessels, significantly reduce the anterior and posterior load of the myocardium and relieve angina pectoris, but also effectively inhibit the aggregation and adhesion of platelets, demonstrating significant antithrombotic efficacy. According to relevant studies, nitrate drugs also have significant effects in controlling patients' portal hypertension, effectively preventing the risk of varicose vein haemorrhage, and greatly enhancing the overall therapeutic effect of patients [31] .

Nitrates are not isolated in their role in the cardiovascular system; they also have an impact on bone metabolism. As donors of nitric oxide, nitrates inhibit bone resorption by decreasing the number and activity of osteoclasts, while at the same time they promote bone formation by promoting osteoblast proliferation, osteocalcin synthesis, and the process of bone mineralisation. A case-control study by Rejnmark et al. [32] found a 15% reduction in the risk of fracture in users of organic nitrates compared to non-users. Jamal et al. [33] A randomised trial demonstrated the beneficial effects of nitrates on bone health in postmenopausal women, not only inhibiting bone resorption but also stimulating bone formation, revealing the potential of nitrates in bone health. In addition, data from in vitro and animal studies have shown that nitric oxide has a significant beneficial effect on bone metabolism [34] , and it is by increasing the release of NO and decreasing the number and activity of osteoclasts that the protective effect of oestrogen on bone is realised. Nitric oxide has also been shown to increase osteoblast proliferation, osteocalcin synthesis, and osteoclast mineralisation in vitro [34] . However, it is worth noting that the role of nitric oxide in the skeletal system is closely related to its concentration. At low concentrations, nitric oxide stimulates osteoblast and osteoclast activity and controls osteoclast-mediated bone resorption. However, at higher concentrations, such as after inducible nitric oxide synthase activation or exogenous administration of higher doses of nitric oxide donors, it may lead to bone loss [34] . Therefore, when applying nitrates to the treatment of OP, we must give due consideration to their dosage, route of administration, and frequency of administration to ensure that they can exert the best therapeutic effect.

2.6. Thiazide Diuretics

Thiazide diuretics, an important member of the antihypertensive drug class, have been in clinical use since the 1950s and continue to be used today. Such drugs have shown significant benefits in the maintenance of cardiovascular health, effectively reducing risks including stroke, heart failure, coronary events and death. Their mechanism of action is mainly through the action of Na-Cl co-transporter proteins in the distal tubules of the renal units, using diuresis and reduction of blood volume to lower blood pressure. Long-term use of thiazides also has the efficacy of lowering blood pressure through peripheral vasodilatation [35] .

Thiazides have also demonstrated significant efficacy in regulating calcium homeostasis and enhancing bone density. Inhibition of sodium chloride co-transporter protein in distal tubules significantly reduces urinary calcium excretion, which in turn promotes intestinal calcium absorption and inhibits parathyroid hormone secretion, thus effectively reducing bone resorption [36] . At the same time, thiazides also act directly on osteoblasts, not only stimulating osteoblast differentiation, but also inhibiting osteoclast bone resorption activity by inhibiting carbonic anhydrase [37] . Van der Burgh et al. [38] noted in a cross-sectional study that thiazide diuretics had a significant positive effect on lumbar spine bone density in the general population. xiao et al. [39]) cohort study found a significant 14% reduction in all fracture risks in thiazide diuretic users compared to non-users, highlighting the significant protective effect of thiazides in fracture risk prevention and control. Dvorak et al. [40] observed in an in vitro experiment that thiazides did not have a direct effect on osteoclast proliferation in human and 2-month-old rat bone, but did directly stimulate RUN related transcription factor 2 and bone bridging protein production, both key markers of osteoblast differentiation. An in-depth study based on a Swedish database demonstrated that the use of either benfluothiazide or hydrochlorothiazide significantly reduced the risk of hip fracture, further revealing a strong link between the choice of antihypertensive medication and fracture risk [41] .

3. Impact of anti-OP drugs on CVD

3.1. Vitamin D

Vitamin D, an essential steroid hormone, exists in two main forms, vitamin D2 and vitamin D3. Vitamin D2 is mainly derived from ergocalciferol in plants, while vitamin D3 is mainly derived from cholecalciferol in animal foods, and both forms play a significant role in the human body [42] . Vitamin D not only promotes intestinal reabsorption of calcium, but also binds tightly to the vitamin D receptor in bone cells, which promotes calcium and phosphorus deposition in the bones, thus reinforcing the structure and strength of the bones. In addition, vitamin D can also directly affect the parathyroid gland, stimulating the production and secretion of parathyroid hormone, which regulates calcium and phosphorus metabolism, maintains the calcium-phosphorus balance in the body, and builds a solid barrier for bone health [43] . Therefore, vitamin D supplementation has become an effective preventive measure for elderly patients with osteoporosis. The Primary Osteoporosis Guidelines (2022) also clearly states that for people with vitamin D deficiency or insufficient intake of vitamin D, vitamin D intake should be actively increased to ensure that the serum 25(OH)D level is maintained at more than 50 nmol/L, which is of vital significance to the maintenance of bone health [44] .

Vitamin D displays pleiotropic effects in the cardiovascular system mediated through intracellular vitamin D receptors or other transmembrane receptors that effectively modulate senescence, inflammation, aging, and adipopathy [45] . In the Randomised, Double-Blind, Placebo-Controlled Trial of Monthly Vitamin D, Thompson et al. [46] provided insight into the effects of intermittent vitamin D supplementation and found that five years of sustained vitamin D supplementation may significantly reduce the incidence of major cardiovascular events, in particular the risk of myocardial infarction and coronary artery haemodilution. This finding further highlights the importance of vitamin D in maintaining human health.

However, some clinical studies have failed to unequivocally demonstrate a significant positive effect of vitamin D supplementation on cardiovascular health [47] , and there is still a need for more refined randomised controlled trials and systematic reviews to reveal the reasons

behind this.

3.2. Bisphosphonates

Bisphosphonates occupy a central position in the treatment of bone diseases and abnormal calcium metabolism. It binds to hydroxyphosphatidylcholine in the bone, effectively inhibits osteoclast activity and significantly slows down the process of bone resorption, and is widely used in the treatment of a variety of diseases such as OP, metaplastic osteitis, as well as hypercalcaemia and osteodynia caused by bone metastases from malignant tumours. In China, oral bisphosphonates, such as alendronate and risedronate, are generally recommended as the preferred treatment option for patients with low to moderate fracture risk. Authoritative guidelines in the United States and Europe also include bisphosphonates as an initial treatment option for OP. In the Swiss guidelines, oral bisphosphonates are considered a powerful follow-up therapy for intermediate-risk postmenopausal patients after treatment with selective oestrogen receptor modulators.

Possible mechanisms by which bisphosphonates affect atrial conduction include interference with intracellular electrolyte stabilisation, enhancement of pro-inflammatory responses, promotion of fibrosis and anti-angiogenic effects. Studies have demonstrated that administration of atherogenic diets containing bisphosphonates to vertebrates (e.g. pigeons, monkeys, etc.) significantly reduces atherosclerotic plaques, improves arterial elasticity, reduces systemic vascular resistance and carotid intima-media thickness, and overall reduces intravascular calcification [48] .

However, the relationship between bisphosphonates and CVD is complex. On the one hand, their potential protective effect against atherosclerosis is highly praised; on the other hand, their possible increase in the risk of atrial fibrillation has attracted widespread attention [48] . Systematic evaluations and meta-analyses have shown that bisphosphonates may increase the risk of atrial fibrillation, e.g., the risk of arrhythmia, especially atrial fibrillation, was increased in the zoledronate group compared with the placebo group, and there was no significant correlation with the duration of drug exposure [49] . Therefore, further studies and validation are needed regarding the combined cardiovascular effects of bisphosphonates.

3.3. Oestrogen

From the beginning to the end of skeletal development, in both men and women, oestrogen plays a key role in ensuring that the epiphyseal growth plates close in accordance with their intended physiological course. Estrogen plays a pivotal role in the regulation of skeletal growth, maturation, and bone turnover in the adult skeleton. In young skeletal tissue, oestrogen deficiency significantly contributes to the proliferation of osteoclasts and the enhancement of bone resorption activity. As individuals enter menopause, estrogen loss further exacerbates bone loss in cancellous and cortical bone. Estrogen functions by finely regulating the number of osteoblasts and osteoclasts in the bone marrow. By binding to the oestrogen receptor, it stimulates the expression of osteoprotegerin and inhibits the function of nuclear factor-κB receptor-activating factor ligand, thereby inhibiting osteoclast formation and reducing bone resorption. Estrogen also activates the Wnt/β-catenin signalling pathway, intensifies osteoblast activity and promotes the transformation of MSCs to osteoblasts by upregulating BMP signalling. It also promotes the anti-apoptotic process of osteoblasts and osteoclasts, thus effectively controlling the rate of bone remodelling and maintaining the delicate balance between bone filling and bone resorption [50,51] .

Estrogen significantly reduces serum cholesterol levels, inhibits abnormal proliferation of vascular smooth muscle cells, induces autophagy in vascular endothelial cells, and significantly enhances the antioxidant properties of blood vessels and reduces the accumulation of lipids within the vasculature [52] , which dramatically reduces the risk of atherosclerosis and provides a solid barrier for the cardiovascular system. In perimenopausal women, plasma levels of total cholesterol and LDL cholesterol are significantly elevated after the decline in oestrogen levels, whereas HDL cholesterol levels are significantly reduced. This disturbed state of lipid metabolism is a key factor in the promotion of atherosclerosis and cardiovascular events [53] . The study by Anne et al. [54] further provides strong evidence for the cardioprotective effects of oestrogen. By simulating ischaemia-reperfusion injury, they found that oestrogen can significantly reduce the damage suffered by the heart due to ischaemia, demonstrating its excellent cardioprotective ability.

3.4. Parathyroid Hormone Analogues

Chinese guidelines [55] advocate the use of thyroid hormone analogues, such as teriparatide, with the aim of significantly increasing bone density and thus reducing the risk of vertebral and non-vertebral fractures. The N-terminus of parathyroid hormone binds precisely to the parathyroid hormone receptor 1 on bone and kidney, which has a significant impact on osteogenesis, while its C-terminus interacts with another class of receptors in a complex manner and exhibits a wide variety of biological functions, such as the regulation of osteoclast apoptosis [56] . This was further confirmed by experiments of Wang et al. [57] . After treating primary osteoblast cultures derived from transgenic mice with parathyroid hormone for one week, osteoblast progenitor cells showed significant proliferation and differentiation, while apoptosis of osteoblasts was effectively inhibited. Parathyroid hormone may be the drug of choice for patients at high risk of fracture and for whom other OP therapies (e.g., bisphosphonates) are ineffective or intolerable.

Abnormally elevated levels of parathyroid hormone can disrupt calcium homeostasis, and by elevating intracellular calcium levels, high levels of PTH adversely affect mitochondrial function, ATP production, and oxidative stress and inflammatory states, which may ultimately lead to damage or even necrosis of cardiomyocytes. This in turn may lead to pathological conditions such as arrhythmias [58] . According to the results reported in several studies, the concentration of parathyroid hormone is generally elevated in a wide range of cardiac and renal diseases, especially in hyperparathyroidism, which produces significant adverse effects on the heart and cardiomyocytes, such as symptoms of cardiac hypertrophy, remodelling and arrhythmias. By lowering PTH levels and activating calcium-sensitive receptors on parathyroid tissue, it has been widely demonstrated to provide significant protection to the cardiovascular system [59] . Therefore, parathyroid hormone analogues should be used with caution in OP patients with concomitant CVD.

3.5. Calcitonin

Calcitonin, a hormone synthesised by the thyroid gland, inhibits osteoclast activity and reduces the release of bone calcium and bone phosphorus, and is one of the commonly used OP drugs [60] . Salmon calcitonin has the highest potency of all the calcitonins and has become the drug of choice for clinical use [61] . A five-year study showed that 200 IU of salmon calcitonin nasal spray per day significantly reduced the risk of new vertebral fractures in postmenopausal women with osteoporosis [62] .

Calcitonin is also used in the treatment of hypercalcaemia, effectively alleviating problems such as hypertension and arrhythmias caused by hypercalcaemia by inhibiting osteolysis and enhancing renal excretion of calcium [61] . A study by Moreira et al. [63] , further revealed that global disruption of calcitonin receptor signalling in mice leads to atrial fibrosis and increased susceptibility to atrial fibrillation. However, in clinical practice, calcitonin may be accompanied by a range of adverse effects such as tachycardia with hypotension [64] . Currently, rational combination strategies are used in clinical practice to improve the therapeutic efficiency and mitigate the cardiovascular adverse effects in patients with OP [65] .

3.6. Monoclonal Antibodies

The specific binding of deslumizumab to nuclear factor-κB receptor activator ligand provides a reliable therapeutic pathway for the treatment of OP. As a classical monoclonal antibody in the field of anti-bone resorption, desutumumab has been widely used in the treatment of OP since 2010, and its ability to significantly enhance bone mineral density and reduce the risk of fracture at key skeletal sites has been demonstrated in several clinical studies [66,67] . There is also interest in the potential of desutumumab for CVD protection. Studies have shown that users of deslumizumab show low ORs in a wide range of CVDs, suggesting that it may be potentially protective against all CVDs [68] .

Another drug, romotuzumab, a novel drug monoclonal antibody against sclerostin encoded by the SOST gene, has shown significant therapeutic effects in promoting bone formation and inhibiting bone resorption since its application in Japan in 2019 [69] . However, there is also a potential risk of cardiovascular adverse events in practical application. According to the ARCH trial, the risk of cardiovascular events was increased in patients treated with romotuzumab [70] . Sixty-eight patients have reported adverse cardiovascular events associated with romotuzumab in initial clinical use [71] . Currently, there is controversy regarding the correlation between monoclonal antibodies and cardiovascular risk. Given the short time since the drug was introduced, the insufficient research related to cardiovascular risk and the limitations of the existing studies, further clinical studies with larger samples are needed to confirm its role in the non-skeletal aspects of OP patients.

4. Summary

The incidence of CVD and OP both increase with age and are potentially linked. Currently, drugs for OP and anti-CVD drugs are widely used in the clinic, and the effects of drugs for one disease on the other when acting on the relevant targets are debated and the mechanisms are complex. β-blockers, statins, renin-angiotensin system inhibitors, calcium antagonists, nitrates, and thiazide diuretics are among the anti-cVD drugs that have varying degrees of effect on osteoporosis. The effects of some drugs and their mechanisms have been gradually clarified, but there are still many issues that require further in-depth studies, more conclusive evidence and more randomised controlled trials and systematic reviews to clarify the effects of drugs on cardiovascular metabolism in the treatment of one disease over another. treatment of one disease on another, in order to provide a more reliable basis for clinical treatment and patient health. Meanwhile, Q Given the interaction between CVD and OP in terms of drug treatment, future treatment strategies should focus more on the combination of the two. On the one hand, for patients suffering from both CVD and OP, doctors should fully consider drug-drug interactions when choosing therapeutic drugs and avoid using drugs that may aggravate the other disease. On the other hand, for patients who have already received CVD treatment, their bone mineral density, blood calcium and other indicators should be monitored regularly, so that osteoporosis can be detected and dealt with in a timely manner. Meanwhile, patients who have received OP therapy should also be concerned about their cardiovascular health, and their treatment regimen should be adjusted in time to reduce the occurrence of cardiovascular events.

Table 1. Effect of Anti-cardiovascular Disease Drugs on Osteoporosis

Name	Impact on OP	Note
Beta-blocker	Effects of blocking endogenous catecholamines on beta-adrenergic receptors	Increased risk of fracture
Statins	Enhanced bone morphogenetic protein gene expression Promotes bone formation and enhances bone density	Differences in the mechanism of action during bone conversion
Renin-angiotensin system inhibitors	ACEIs Increase Bone Density and Reduce Fracture Risk RAS Inhibitors Increase Bone Mass and Alleviate Osteoporosis Symptoms	
Calcium antagonist	Significantly reduces OP risk and boosts bone density	Negative effects on bone metabolism
Nitrate drugs	Reduces osteoclast number and activity Promotes osteoblasts value-added and bone mineralisation	High concentrations lead to bone loss
Thiazide diuretics	Enhances bone density and stimulates osteoblast differentiation Inhibits osteoclast activity and reduces bone resorption	

Table 2. Effect of anti-osteoporosis drugs on cardiovascular diseases

Name	Impact on CVD	Note
Vitamin D	Reduced risk of myocardial infarction and coronary revascularisation	Some studies have failed to prove a positive effect
Bisphosphonates	Reduces atherosclerotic plaque and improves arterial elasticity Reduction of intravascular calcification	Increased risk of atrial fibrillation
Oestrogen	Enhances vascular antioxidant properties Reducing the risk of atherosclerosis	
Parathyroid hormone analogue	Abnormally elevated levels can disrupt calcium homeostasis, leading to heart problems such as damage to heart muscle cells and arrhythmias.	Osteoporosis patients with concomitant cardiovascular disease should be used with caution
Calcitonin	Enhancement of renal excretion of calcium and treatment of hypercalcaemia	Adverse effects such as tachycardia and hypotension are present.
Monotherapy	Dexuzumab shows potential for CVD protection, with users demonstrating lower odds in a variety of CVDs	Romolizumab treatment may increase risk of cardiovascular events

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